Huisgen and R. Schug, *J. Chem. Soc., Chem. Commun.*, 59 (1975); (i) *ibid.*, 60 (1975); (j) I. Karle, J. Flippen, R. Huisgen, and R. Schug, *J. Am. Chem. Soc.*, **97**, 5285 (1975); (k) R. Huisgen, *Acc. Chem. Res.*, **10**, 117, 199 (1977).
(2) (a) T. Okuyama, T. Fueno, H. Nakatsuji, and J. Furukawa, *J. Am. Chem. Soc.*, **89**, 5826 (1967); (b) T. Fueno, I. Matsumura, T. Okuyama, and J. Furukawa, *Bull. Chem. Soc. Jpn.*, **41**, 818 (1968); (c) *J. Polym. Sci., Part A-1*, **7**, 1447 (1969); (d) T. Okuyama, T. Fueno, and J. Furukawa, *Tetrahedron*, **25**, 5409 (1969); (e) T. Okuyama and T. Fueno, *J. Org. Chem.*, **39**, 3156 (1974); (f) T. Okuyama, M. Nakada, and T. Fueno, *Tetrahedron*, **32**, 2249 (1976); (g) T. Okuyama, M. Masago, M. Nakada, and T. Fueno, *ibid.*, **33**, 2379 (1977).
(3) J. K. Williams, D. W. Wiley, and B. C. McKusick, *J. Am. Chem. Soc.*, **84**, 2210 (1962).
(4) P. D. Bartlett, *Q. Rev., Chem. Soc.*, **24**, 473 (1970).
(5) W. M. Schubert, B. Lamm, and J. R. Keeffe, *J. Am. Chem. Soc.*, **86**, 4727 (1964).
(6) J. P. Kennedy in "Copolymerization", G. E. Ham, Ed., Interscience, New York, 1964, p 308.
(7) T. Fueno, O. Kajimoto, K. Izawa, and M. Masago, *Bull. Chem. Soc. Jpn.*, **46**, 1418 (1973); O. Kajimoto, M. Kobayashi, and T. Fueno, *ibid.*, **46**, 1422, 1425, 2316 (1973).
(8) R. Bolton in "Comprehensive Chemical Kinetics", Vol. 9, C. H. Bamford and C. F. H. Tipper, Ed., Elsevier, Amsterdam, 1973, Chapter 1.
(9) T. Fueno, *Chem. Rev. (Jpn.)*, **1**, 35 (1973).
(10) T. Fueno and Y. Yonezawa, *Bull. Chem. Soc. Jpn.*, **45**, 52 (1972).
(11) T. Fueno and Y. Yamaguchi, *Bull. Chem. Soc. Jpn.*, **45**, 3290 (1972).

Synthesis of Thermodynamically Less Stable Enol Thioethers. An Alternative Oxidative Decarboxylation of α-Thio Acids

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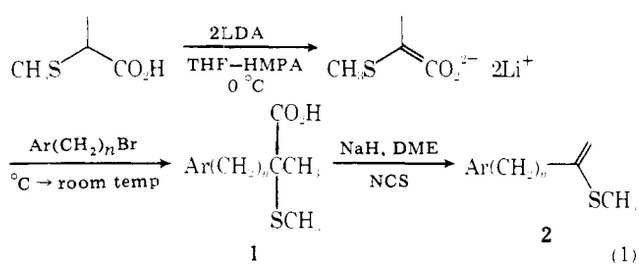
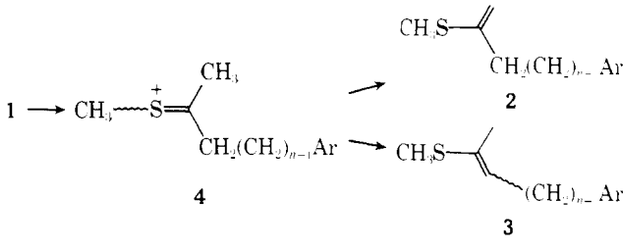
Enol thioethers, valuable synthetic intermediates, normally arise by elimination reactions from the corresponding thioketals (or thioacetals).[1] Such reactions generally proceed under thermodynamic control. Regiocontrolled synthesis via a Wittig-type[2] or Peterson-type[3] olefination is limited. During our investigations of the oxidative decarboxylation of α-methylthiocarboxylic acids,[4,5] we discovered a new approach to achieve this type of transformation and which provides direct access to the thermodynamically less stable enol thioethers.

The requisite substrates were readily available by the alkylation of the dianion of 2-methylthiopropionic acid[6] with an alkyl bromide as summarized in eq 1 and Table I. Treatment of the sodium salts of the acids **1** with 1 equiv of *N*-chlorosuccinimide (NCS) in anhydrous DME led cleanly to the desired enol thioethers **2**. No detectable amounts of the alternative regioisomers are seen. That **2** represents the thermodynamically less stable enol thioethers is reflected by the rapid equilibration to the more substituted enol thioethers **3** upon treatment of **2** with anhydrous acid.

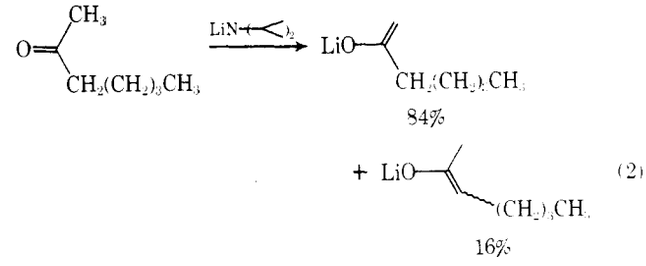


1 2 (1)

The regiochemistry presumably reflects kinetic deprotonation of the thionium intermediate **4**. This strikingly high

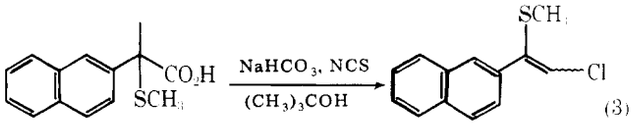


regioselectivity may be contrasted to the kinetic enolate generation from 2-heptanone in which only an approximately 5:1 selectivity for deprotonation of the methyl group is observed (eq 2).[7] While the differences can be attributed to a



(2)

variety of factors, including the differences in base and the effect of the stereochemistry of the thionium species, no convincing arguments can be seen. Synthetically, since the enol thioether can be an enolate or enol equivalent in some types of reactions, this selectivity can be very useful. These results also contrast with our earlier observations[4] in which the chlorinated vinyl sulfide (eq 3) was obtained when *tert*-

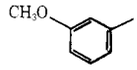
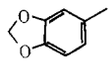
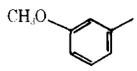
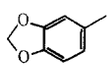


(3)

butyl alcohol was employed as solvent. Presumably, the lower oxidation potential of NCS in an aprotic nonpolar solvent like DME accounts for the greater selectivity in the present cases.

Thus, this new reaction makes 2-methylthiopropionic acid equivalent to the vinyl anion **5** and thus an alternative for the

Table I. Oxidative Decarboxylation Route to Vinyl Sulfides (see eq 1)

entry	Ar	*n*	yield 1, %	registry no.	2, %	registry no.
1	Ph	2	57	67556-31-4	82	67556-36-9
2	Ph	3	60	67556-32-5	85	67556-37-0
3		3	66–85	67583-96-4	84–100	67556-38-1
4		3	71–90	67556-33-6	85–86	67556-39-2
5		4	74–95	67556-34-7	85	67556-40-5
6		5	74	67556-35-8	85	67556-41-6

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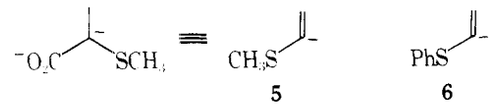
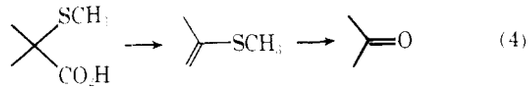


5 6

vinyl phenyl sulfide anion **6**.[8] The generality of this reaction and the ease of hydrolysis of vinyl methyl sulfides (in contrast to vinyl aryl sulfides) make this approach (eq 4) a valuable



(4)

alternative to the oxidative decarboxylation in alcohol solvents.

Experimental Section

All reactions were run under a positive pressure of dry nitrogen in an apparatus that was flame-dried in a nitrogen stream. In experiments requiring dry solvents, DME and THF were freshly distilled from sodium benzophenone ketyl. Benzene, dimethyl disulfide, diisopropylamine, pyridine, and HMPA were all distilled from calcium hydride. Thin- and thick-layer chromatographic plates employed Macherery Nagel (Duren) MN-Kieselgel P/UV 254 activated by drying at 140 °C for 2 h. Column chromatography employed W. R. Grace silica gel, grade 62, 60–200 mesh. Melting points (obtained on a Thomas-Hoover apparatus) and boiling points are uncorrected.

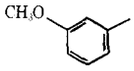
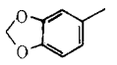
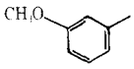
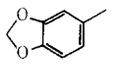
Infrared spectra were recorded on a Perkin-Elmer 267 spectrophotometer. NMR spectra were obtained on a Varian EM-360 or Jeolco MH-100 spectrometer. Chemical shifts are given in parts per million (δ) downfield from internal Me_4Si with coupling constants in hertz. Splitting patterns are designated s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and b = broad. Mass spectra were obtained on an AEI MS-902 high-resolution mass spectrometer at an ionizing voltage of 70 eV and an ionizing current of 100 mA.

Alkylation of 2-Methylthiopropionic Acid. Preparation of 2-Methyl-2-methylthio-5-(3,4-methylenedioxyphenyl)pentanoic Acid. To a solution of 180 mmol of lithium diisopropylamide [from 19.21 g (190 mmol) of diisopropylamine and 180 mmol of *n*-butyllithium] in hexane in 100 mL of dry THF at 0 °C was added 9.48 g (79.0 mmol) of 2-methylthiopropionic acid in 100 mL of HMPA. After 4 h at 0 °C, 23.73 g (98 mmol) of 1-bromo-3-(3,4-methylenedioxyphenyl)propane was added all at once followed by additional HMPA to maintain homogeneity. The reaction was stirred overnight, during which time it warmed to room temperature. It was quenched with water and extracted with ether, and the ether layer was washed with saturated aqueous sodium carbonate. The combined water layers were acidified to pH 1 with concentrated hydrochloric acid and extracted with ether. The resultant ether solution was washed with water and saturated aqueous sodium chloride and dried over anhydrous magnesium sulfate. The residue, after concentration, was chromatographed on a 6.5 × 60 cm column of silica gel utilizing 2:1 hexane–acetone to give 15.75 g (71% yield) of product, mp 58–60 °C (unrecrystallized). Yields up to 90% (on an approximately 10-mmol scale) were obtained by this procedure: IR (CCl_4) 3300–2800, 1700, 1505, 1490 cm^{-1}; NMR (CCl_4) δ 1.40 (3 H, s), 1.70 (4 H, m), 2.07 (3 H, s), 2.55 (2 H, t, J = 6 Hz), 5.88 (2 H, s), 6.63 (3 H, m), 12.08 (1 H, s); MS *m/e* (relative %) 282 (33), 221 (64), 189 (10), 149 (13), 148 (100), 136 (14), 135 (93), 91 (12), 77 (14), 45 (26). Anal. Calcd for $C_{14}H_{18}O_4S$: 282.0926. Found: 282.0915.

The remaining examples are summarized in Table II. The spectral data for these cases appear as supplementary material.

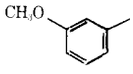
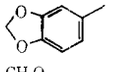
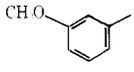
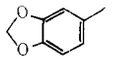
Oxidative Decarboxylation. Preparation of 5-(3,4-Methylenedioxyphenyl)-2-methylthio-1-pentene. A solution of 162.3 mg (0.575 mmol) of 2-methyl-2-methylthio-5-(3,4-methylenedioxyphenyl)pentanoic acid in 10 mL of dry DME was added to a suspension of 0.673 mmol of sodium hydride (washed free of mineral oil) in

Table II. Reaction Details for Alkylation [a]

Ar	*n*	LDA, mmol	CH_3SCHCO_2H, wt (mmol)	THF, mL	HMPA, mL	$Ar(CH_2)_nBr$, wt (mmol)	registry no.	product, wt (% yield)	mp, °C
Ph	2	38.4	1.92 g (16.0)	20	15	2.73 g (20.1)	103-63-9	2.03 g (57)	75–76
Ph	3	24	1.20 g (10)	12.5	12.5	1.82 g (12.5)	637-59-2	1.42 g (60)	55–56 [b]
	3	19.3	967 mg (8.05)	10	10	2.50 g (10)	6943-97-1	1.84 g (85)	
	3	18.9	943 mg (7.85)	10	10	2.36 g (9.71)	28437-31-2	1.99 g (90)	58–60 [b]
	4	19.0	951 mg (7.93)	10	10	2.33 g (9.59)	23464-42-8	2.12 g (95)	
	5	5.26	662 mg (2.19)	4	3	662 mg (2.44)	67556-42-7	432 mg (64)	

[a] Also see the text. [b] Material solidifies upon evaporation of solvent. Melting point is reported for this material without recrystallization.

Table III. Reaction Details for Oxidative Decarboxylation

Ar	*n*	acid, wt (mmol)	NaH, mmol	NCS, wt (mmol)	DME, mL	product, wt (% yield)
Ph	2	150 mg (0.669)	0.741	108.9 mg (0.816)	15	98.1 mg (82)
Ph	3	114 mg (0.480)	0.561	75.1 mg (0.562)	15	78.4 mg (85)
	3	134 mg (0.50)	0.52	80 mg (0.60)	10	111 mg (100)
	3	see the text				
	4	155 mg (0.551)	0.610	89.7 mg (0.672)	15	111 mg (85)
	5	131 mg (0.421)	0.423	62.0 mg (0.465)	15	94.4 mg (85)

5 mL of dry DME at room temperature. Upon cooling to 0 °C, 90.0 mg (0.647 mmol) of NCS was added all at once and stirring was continued for 1 h at 0 °C. The reaction mixture was poured into water and extracted with ether. The ether layers were washed with water and then with 10% aqueous sodium sulfite and dried. After evaporation in vacuo, the residue was passed through a 2 × 5 cm column of silica gel utilizing 5% ether in hexane to give 115 mg (85%) of the vinyl sulfide: IR (CCl_4) 1595, 1485, 940, 840 cm^{-1}; NMR (CCl_4) δ 1.80 (2 H, m), 2.16 (5 H, s + m), 2.49 (2 H, t, J = 7 Hz), 4.49 (1 H, s), 4.92 (1 H, s), 5.82 (2 H, s), 6.56 (3 H, m); MS m/e (relative %) 236 (10), 149 (9), 148 (100), 147 (7), 135 (33), 101 (28), 77 (9), 51 (6). Anal. Calcd for $C_{13}H_{16}O_2S$: 236.0871. Found: 236.0867.

The remaining examples are summarized in Table III. The spectral data for these cases appear as supplementary material.

Acknowledgment. We wish to thank the National Science Foundation and the National Institutes of Health (General Medical Sciences) for their generous support of our programs. D.B. was a NSF-URP participant (1977). M.J.C. wishes to thank the Science Research Council for a postdoctoral fellowship.

Registry No.—2-Methylthiopropionic acid, 58809-73-7.

Supplementary Material Available: Spectral data for additional examples of alkylation of 2-methylthiopropionic acid and oxidative decarboxylation (3 pages). Ordering information is given on any current masthead page.

References and Notes

(1) T. Cohen, G. Herman, J. R. Falck, and A. J. Mura, Jr., *J. Org. Chem.*, **40**, 812 (1975).
(2) M. Green, *J. Chem. Soc.*, 1324 (1963); I. Shahak and J. Almog, *Synthesis*, 145 (1970); J. I. Grayson and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 2263 (1977).
(3) F. A. Carey and A. S. Court, *J. Org. Chem.*, **37**, 939 (1972).
(4) B. M. Trost and Y. Tamaru, *J. Am. Chem. Soc.*, **97**, 3528 (1975); *Tetrahedron Lett.*, 3797 (1975); *J. Am. Chem. Soc.*, **99**, 3101 (1977).
(5) B. M. Trost and G. Lunn, *J. Am. Chem. Soc.*, **99**, 7079 (1977).
(6) Cf. B. M. Trost and K. K. Leung, *Tetrahedron Lett.*, 4197 (1975); K. Iwai, M. Kawai, H. Kosugi, and H. Uda, *Chem. Lett.*, 385 (1974).
(7) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).
(8) R. C. Cookson and P. J. Parsons, *J. Chem. Soc., Chem. Commun.*, 990 (1976); B. Harirchian and P. Magnus, *ibid.*, 522 (1977).

Evidence for Ipso Attack in the Peroxodisulfate Oxidation of Tertiary Aromatic Amines

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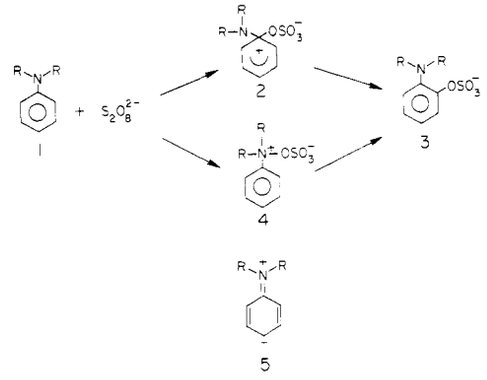
Studies from two laboratories have shown that the reaction between peroxodisulfate ions and aromatic amines (the Boyland–Sims oxidation) proceeds via electrophilic attack of the peroxodisulfate ion on the neutral amine.[1-5] Since the product is the *o*-aminoaryl sulfate (**3**) (the para isomer is only formed in significant quantity when both ortho positions are blocked),[6] the arylhydroxylamine-*O*-sulfonate (**4**) was proposed as an intermediate.[2] This proposal was supported by kinetic substituent effects which excluded rate-limiting attack at the ortho-carbon atom.[2,3] This proposal was also consistent with Boyland and Nery's observations on the stability of phenylhydroxylamine-*O*-sulfonate (**4**, R = H).[7] This compound, although stable enough to be isolated, rearranges to the ortho sulfate in acid and also during workup under neutral conditions. The related substance, *N*-acetyl-2-naphthylhydroxylamine-*O*-sulfonate also rearranges to the ortho sulfate at neutrality.[8] Other related rearrangements have been reported.[9]

Edward and Whiting,[10] however, synthesized **4**, R = Me, by reaction of *N,N*-dimethylaniline *N*-oxide with sulfur trioxide and showed that it did not rearrange to the ortho sulfate under Boyland–Sims conditions. Rather, it underwent hydrolysis to the parent *N*-oxide and sulfate ions. This finding excluded **4**, R = Me, as intermediate although previous work



had shown that the tertiary amines gave the expected ortho sulfate upon reaction with peroxodisulfate ions.[4,6]

Since the substituent effects which excluded rate-limiting attack at the ortho-carbon atom had been conducted only on primary amines, we carried out similar kinetic studies on two sets of ring-substituted *N,N*-dimethylanilines. These data are shown in Table I. They exclude rate-limiting attack at the ortho-carbon position for the tertiary amines as well since both the 2,4-dimethyl- and the 2-methyl-4-chloro-*N,N*-dimethylanilines react more rapidly than the corresponding 2,3 isomers. The opposite relative reactivity would be observed were rate-limiting attack at the ortho carbon.[2] The apparent discrepancy between Edward and Whiting's result and our present data may be rationalized by postulating ipso attack[11] with rearrangement via **2** to account for the formation of the ortho sulfate in the case of the tertiary amines. Ipso attack may also be involved for the primary and secondary amines,

Table I. Comparison of the Rates of Oxidation of 2,3- and 2,4-Disubstituted *N,N*-Dimethylanilines by Peroxodisulfate Ions[a]

compd	registry no.	no. of runs	concn range, 10^2 M	$10^3 k'$, min^{-1}	k, M^{-1} min^{-1}
2-methyl-4-chloro-*N,N*-dimethylaniline	67761-87-9	4	2.1–4.4	2.17–4.95	0.107 ± 0.008
2-methyl-3-chloro-*N,N*-dimethylaniline	67761-88-0	6	2.2–3.4	1.17–2.2	0.0575 ± 0.006
2,4-dimethyl-*N,N*-dimethylaniline	769-53-9	3	2–8	3.2–12.8	0.153 ± 0.002
2,3-dimethyl-*N,N*-dimethylaniline	24226-35-5	4	2–7.5	2.7–8.7	0.129 ± 0.01

[a] Reaction conditions: 30 °C, 0.1 M KOH in 50% ethanol–water (v/v), the initial amine–peroxodisulfate ratio was 10. Second-order rate constants were calculated by division of the pseudo-first-order constants by the initial concentration of the amine. Ethanol is not oxidized by peroxodisulfate at a significant rate at 30 °C.

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